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LEGAL DEPARTMENT
INCYTE GENOMICS, INC.
3160 PORTER DRIVE
PALO ALTO, CA 94304

| EXAMINER |
|---|
| HARRIS, ALANA M |

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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Paper No. 23

Application Number: 09/397,558
Filing Date: September 16, 1999
Appellant(s): LAL et al.

Terence P. Lo, Ph.D.
For Appellant

**SUPPLEMENTARY EXAMINER'S ANSWER**

This is in response to appellant's brief on appeal filed August 17, 2001.

The Examiner's Answer mailed December 7, 2001 (Paper number 23) has been vacated and a supplementary Examiner's Answer is set forth below due to a typographical error by the Examiner. Correction has been made on page 7 and the Examiner is in agreement with the Appellants as to how the claims fall or stand. No new issues have been raised.

***(1) Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

***(2) Related Appeals and Interferences***

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

***(3) Status of Claims***

The statement of the status of the claims contained in the brief is correct.

***(4) Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

***(5) Summary of Invention***

The summary of invention contained in the brief is correct.

***(6) Issues***

The appellant's statement of the issues in the brief is correct.

***(7) Grouping of Claims***

As to Issue 1

All of the claims on appeal are grouped together.

As to Issue 2

All of the claims on appeal are grouped together.

As to Issue 3

Claim 2 is grouped by itself.

As to Issue 4

All of the claims on appeal are grouped together.

***(8) Claims Appealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

***(9) Prior Art of Record***

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

***(10) Grounds of Rejection***

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 U.S.C. § 101***

Claim 1, 2, 21, 22 and 27-29 are rejected under 35 U.S.C. 101. This rejection is set forth in prior Office Action, Paper No. 13 mailed February 9, 2001. These claims are rejected under this statute because the claimed invention is not supported by either a specific, substantial asserted utility, a credible or a well established utility.

As stated therein, the instant application has provided a description of two prostate growth-associated membrane proteins (PGAMP) comprising the amino acid sequences of SEQ ID NO:1 (PGAMP-1), SEQ ID NO:2 (PGAMP-2) and claimed fragments of the said sequences. The instant application does not disclose the biological role of this protein or its significance. The instant application asserts that it provides compositions for the diagnosis, prevention and treatment of disorders associated with cell proliferation, particularly cancer. On pages 25 and 26 there are lists of a plethora of organ systems in which cell proliferation disorders can affect, as well as resulting diseases and disorders. The specification asserts that disorders associated with aberrant cell proliferation and cell death can be treated or prevented by administration of agonists, antagonists or inhibitors of PGAMP.

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance because the specification fails to disclose any particular function of biological significance for the

PGAMP. The disclosed protein is alleged to have a potential function in neoplastic and reproductive disorders based upon its expression pattern. PGAMP-1 is expressed in cancerous or hyperplastic prostate (48%) and breast (7%) and in brain and adrenal gland. Whereas, PGAMP-2 shares chemical and structural similarity with a fragment of the mouse apoptosis-associated tyrosine kinase and human PSA. This protein is also expressed in cancerous or hyperplastic prostate (28%) and breast (10%) and in uterus, ovary and colon. However, it would require more research to establish the correlation between actual function and alleged function. After further research, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the

> public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to proteins of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the PGAMP proteins of the instant application were, as of the filing date, useful for diagnosis, prevention and treatment of neoplastic and reproductive disorders as stated at pages 25 and 26 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as PGAMP-1 and PGAMP-2, or the genes encoding them, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

In the absence of definite knowledge of how the PGAMP proteins function, or the biological significance of this protein, there is no immediately evident patentable use for it. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility that, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for PGAMP-1 and PGAMP-2, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Claims 1, 2, 21, 22 and 27-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 U.S.C. § 112***

Claims 1, 2, 21, 22 and 27-29 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation. This rejection is maintained for reasons set forth above in the statement of the grounds of rejection under 35 U.S.C. §101.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 2 is broadly drawn to polypeptides having at least 90% amino acid sequence identity to SEQ ID NO:1 and SEQ ID NO:2. This claim is drawn to a polypeptide sequences that do not contain all of the amino acid residues of SEQ ID NO:1 nor SEQ ID NO:2. Absent evidence to the contrary, these variants are deemed to be incomplete polypeptides. This claim is drawn to a large genus of molecules. In the case of unidentified amino acid residues claimed with open language, the genus of polypeptides comprising only 90% of the known sequences encompasses a variety of subgenera with widely varying attributes. There are 10% in which changes to the polypeptides could exist that render variants that would not possess the specific functions required to make the proteins useful for the application disclosed in the specification. The specification discloses only the structural features of two species, the polypeptide sequences of SEQ ID NO:1 and 2. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed. And as embraced in the 35 U.S.C. 101 rejection, the claimed invention is not supported by either a credible, specific or substantial asserted utility or well established utility as one skilled in the art

would not know how to used the claimed invention so that it would operate as intended without undue experimentation.

***(11) Response to Argument***

Appellants summarize case law on the utility requirement at page 6 of the Brief. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility, as will be explained more fully below.

Appellants argue at pages 7-12 of the Brief that the claimed polypeptides are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established". It is noted that toxicology testing and drug discover are not specifically recited in the specification as originally filed. Each of these uses will be addressed individually, because the facts and issues directed to each use are distinct and separable. First, Appellants argue that toxicology testing is a well-established utility and conclude that the claimed polynucleotides could be used in this manner and that the claimed invention possesses utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case, as indicated at page 8 of the Brief, all nucleic acids and genes are in some combination useful in toxicology testing. Likewise, proteome expression profiling techniques have been developed and polypeptide or polypeptide fragments are known to be expressed are tools essential to any technology that uses proteome expression profiling. However, the particulars of toxicology testing with SEQ ID NO:1 and SEQ ID NO:2 are not disclosed in the instant specification. Potential toxic markers as a indication of a toxic response

are not identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins, but is only potential with respect to SEQ ID NO:1 and 2. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the Appellants' individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this polypeptide could be put.

Appellants argue on page 13 of the Brief that just because the invention belongs to a broad class that does not negate its utility. The instant application does not provide evidence of the claimed polypeptide's function, nor that of similar proteins. While the PTO does issue patents to broad classes there is well-established, substantial a specific utility for those broad classes. As discussed, in the instant case PGAMP-1 has

chemical similarity with CD44 antigen precursor and a Northern analysis shows the expression of the sequence in various libraries. PGAMP-2 along with tow other proteins, mouse apoptosis-associated tyrosine kinase and human prostate specific antigen share six transmembrane regions and the potential signal peptide. While functions of these seemingly homologous proteins have been elucidated, the functions at the time of Appellants filing were not known and are still not known as reinforced by Appellants' Brief. Appellants are merely speculating as to the utility of the claimed invention.

With regard to diagnosis of disease, Appellants argue that the invention has specific utility by virtue of its use in expression profiling. However, in order for a polypeptide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. In the absence of any disclosed relationship between the claimed protein and any disease or disorder and the lack of any correlation between the claimed protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

At page 22 of the Brief, Appellants argue that "a proper *prima facie* case of lack of enablement has not been established." Appellants are reminded that the instant rejection is based on the failure to disclose sufficient properties of the proteins to support an inference of utility. Shared sequence homologies or structural identities

does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

At page 22 in the conclusion section of the Brief, Appellants attest "...that rejections for lack of utility based...on an allegation of 'lack of specificity'... are not supported in the law." Albeit, the utility must be specific, substantial and credible. Appellants' assertion that the claimed invention has utility in toxicology testing, drug development and disease diagnosis do not meet the standards for a specific, substantial, and credible or well-established utility for reasons set forth above.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed

invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

Therefore, for reasons set forth above, Appellants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and it is believed that the rejections should be sustained. For the above reasons, it is believed that the rejections should be sustained. For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Alana M. Harris, Ph.D.
May 3, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600